

WHAT IS CLAIMED IS:

1. A human keratinocyte growth factor (KGF) having an apparent molecular weight of about 28 kDa as determined by migration in NaDodSO<sub>4</sub>/PAGE, and a specific activity of at least about  $3.4 \times 10^4$  units per milligram of protein, where one unit of activity is defined as that amount which causes half of the maximal possible stimulation of DNA synthesis in BALB/MK keratinocyte cells under standard assay conditions.

2. Human KGF according to claim 1, wherein said specific activity is at least about  $3.2 \times 10^5$  units per milligram protein.

3. A bioassay for KGF-like activity in a test sample which comprises the following steps:

- i) growing keratinocytes in culture to confluence and maintaining said confluent culture in serum-free medium;
  - ii) adding a test sample to said confluent culture of keratinocytes;
- and
- iii) determining the stimulation of DNA synthesis in said keratinocytes.

4. A method of producing KGF from cultured cells comprising the following steps:

- i) Culturing KGF-producing cells in culture medium under conditions such that KGF is produced;
- ii) concentrating said culture medium so that a first concentrate is formed;
- iii) contacting said concentrate with heparin under conditions such that KGF present in said first concentrate binds to the heparin whereby a heparin-KGF complex is formed;

- iv) separating said heparin-KGF complex from said concentrate;
- v) treating said heparin-KGF complex under conditions such that said KGF dissociates from the heparin so that a solution of free KGF is formed;
- vi) concentrating said solution so that a second concentrate is formed;
- vii) fractionating said second concentrate so that KGF is separated from the remaining components.

5. A method of producing KGF from cultured cells, according to claim 4, wherein said KGF-producing cells are M426 human embryonic fibroblasts.

6. A DNA segment encoding a human keratinocyte growth factor (KGF) protein.

7. A DNA segment, according to claim 6, wherein said protein has the amino acid sequence defined in Figure II-1.

8. A DNA segment encoding a chimeric KGF-like protein which comprises within a single polypeptide molecule functional segments of human KGF and at least one other polypeptide of the fibroblast growth factor family.

9. A recombinant DNA molecule comprising a DNA segment according to claim 6 or claim 8 and a vector.

10. A culture of cells transformed with said recombinant DNA molecule according to claim 9.

11. A method of producing a human KGF protein comprising culturing said cells according to claim 10 in a culture medium under conditions such that said protein is produced and isolating said protein from said cells.

12. A method of producing a human KGF protein comprising culture said cells according to claim 10 in a culture medium, wherein said protein is secreted from said cell, and isolating said protein from said medium.

13. A human KGF or KGF-like protein having the amino acid sequence in Figure II-1B.

14. A human KGF or KGF-like protein, according to claim 13, which is not glycosylated.

15. An antibody specific for a peptide having the amino acid sequence of human KGF or KGF-like protein, according to claim 13.

16. The antibody according to claim 15 which neutralizes the mitogenic activity of human KGF.

17. A bioassay for expression of a gene encoding KGF, comprising the steps of:

- i) isolating mRNA from tissues or cells;
- and
- ii) annealing said RNA to a DNA probe encoding a human KGF;
- iii) determining the amount of DNA:RNA hybrid containing said DNA probe.

18. A bioassay for KGF antigen comprising the steps of:

- i) extracting polypeptides from body fluids or tissue samples;
- and
- ii) determining the level of human KGF antigen by reaction with an antibody specific for a peptide having the amino acid sequence of human KGF or KGF-like protein, according to claim 13.

19. A pharmaceutical composition for treatment of conditions requiring specific stimulation of epithelial cells, comprising KGF according to claim 1 or claim 13, and an acceptable pharmaceutical carrier.

20. A pharmaceutical composition for treatment of conditions requiring specific inhibition of stimulation of epithelial cells by KGF, comprising antibodies to KGF according to claim 15, and an acceptable pharmaceutical carrier.

21. A method for assaying Keratinocyte Growth Factor (KGF) activity comprising:

- (a) in a first reaction, determining the level of  $^3\text{H}$  thymidine incorporation into DNA after adding an aliquot of a test sample comprising isolated KGF to a culture of keratinocytes grown to confluence and maintained in a serum-free medium;
- (b) in a second reaction, determining the level of  $^3\text{H}$  thymidine incorporation into DNA after adding another aliquot of the test sample of step (a) to a culture of fibroblasts grown to confluence and maintained in a serum free medium; and
- (c) assessing KGF activity by comparing the results of the first reaction with the results of the second reaction, wherein a fold stimulation of  $^3\text{H}$  thymidine incorporation into the DNA in the first reaction that is at least about 50 times greater than in the second reaction indicates KGF activity.

22. An assay for detecting human Keratinocyte Growth Factor (KGF) comprising contacting a test sample suspected of containing KGF with an antibody reactive against KGF and determining the amount of polypeptide antibody complex formed.

23. A method for detecting Keratinocyte Growth Factor (KGF) in a test sample comprising:

- (a) determining the level of  $^3\text{H}$  thymidine incorporation into DNA of keratinocytes after adding, in the presence of a KGF-neutralizing antibody, a test sample suspected of containing KGF to a culture of keratinocytes grown to confluence and maintained in a serum-free medium;
- (b) performing step (a) in the absence of a KGF-neutralizing antibody;

wherein a decrease in  $^3\text{H}$  thymidine incorporation in (a) relative to (b) indicates the presence of KGF in the test sample.